REMARKS

Entry of the foregoing amendments is respectfully requested.

Summary of Amendments

By the foregoing amendments claims 118 and 191 are editorially amended, whereby claims 117-200 continue to be pending, with claims 117, 140, 159, 166 and 180 being independent claims.

Summary of Office Action

The election of species requirement is made final.

Claim 191 is objected to.

Claims 117-119, 134-139, 166, 167, and 175-179 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Fanara et al., U.S. Patent No. 6,699,502 (hereafter "FANARA").

Claims 120-123, 128-133, 140-153, 155-157, 159-165, 168-174, 180-195, and 198-200 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over FANARA in view of Jaeger, U.S. Patent No. 3,914,425 (hereafter "JAEGER").

Claims 124-127, 154, 158, 196 and 197 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over FANARA in view of JAEGER and further in view of Findlay et al., U.S. Patent No. 4,650,807 (hereafter "FINDLAY").

Claims 117-200 are provisionally rejected on the ground of non-statutory obviousness-type double patenting as allegedly being unpatentable of claims of one or more of co-pending

application Nos. 10/736,902, 10/939,351, 11/012,267, 11/115,293 and 11/115,321.

Response to Office Action

Reconsideration and withdrawal of the objection and rejections of record are respectfully requested in view of the foregoing amendments and the following remarks.

Response to Objection to Claim 191

Claim 191 is objected to because of being dependent on itself.

In response, Applicants have amended claim 191 to be dependent from claim 190, thereby rendering this objection moot.

Response to Rejection of Claims under 35 U.S.C. § 103(a) over FANARA alone

Claims 117-119, 134-139, 166, 167, and 175-179 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over FANARA. The Examiner takes the position, *inter alia*, that the subject matter of present claim 117 would allegedly have been obvious to one of ordinary skill in the art in view of FANARA. In this regard, the rejection mainly relies on col. 2, lines 36-50 of FANARA where it allegedly is taught to simultaneously administer more than one active substance and combining the therapeutic effects of active substances with different pharmacokinetic profiles. The rejection asserts that "[i]n order to have the combined therapeutic effects of active substances, it would have been obvious to one with ordinary skill in the art that the period of therapeutic effectiveness of the first active substance would be coextensive with the period of therapeutic effectiveness of the second active substance, especially if the two active substances are related to similar (antitussive) therapeutic activities." Paragraph bridging pages 5

and 6 of the instant Office Action.

Applicants respectfully traverse this rejection for all of the reasons which are set forth in the Appeal Brief filed October 20, 2008 and the Reply Brief filed August 25, 2009. The corresponding remarks are expressly incorporated herein.

It further is pointed out again that the passage of FANARA which the Examiner appears to primarily rely on, i.e., col. 2, lines 36-50, states (emphasis added):

> In parallel, it is increasingly therapeutically advantageous to be able to simultaneously administer by the oral route an active substance released immediately after administration, and the same or a second active substance released gradually and regularly after administration. In the case where the same active substance is simultaneously administered for immediate release and for prolonged release, this makes it possible to rapidly release a sufficient dose of active substance to trigger the desired effect and to maintain this effect by a gradual and prolonged release of the same active substance. In the case where an active substance is released immediately and another active substance is released gradually, this makes it possible to obtain combined therapeutic effects by means of two active substances **having very different pharmacokinetic profiles.**

The Examiner still appears to take the position that in view of the above passage one of ordinary skill in the art allegedly would have an apparent reason to provide a dosage form which comprises two different active substances (having different half-lives), one released immediately after administration and the other one released gradually and regularly after administration, and releases the two active substances in such a manner that the plasma concentration of one active substance is within a therapeutic range over a period which is coextensive with at least about 70 % of the period over which the plasma concentration of the other active substance is within a therapeutic range.

It is noted that the above passage makes reference to active substances which have "very different pharmacokinetic profiles" and can be administered by means of the immediate/controlled release formulations of FANARA. However, FANARA does not explain what exactly is to be understood by the phrase "very different pharmacokinetic profiles". In this

regard, it is pointed out that the term "pharmacokinetic profile" encompasses a wide range of properties of a drug. For example, according to

http://www.nature.com/nrg/journal/v4/n10/glossary/nrg1180_glossary.html (of record) the term "pharmacokinetic profile" is defined as

"[t]he characteristics of a drug that determine its absorption, distribution and elimination in the body".

Applicants submit that in view of the foregoing, it is only with hindsight that one can conclude that the above passage of FANARA renders it obvious to one of ordinary skill in the art to use an immediate/controlled release combination for providing plasma concentrations in a therapeutic range of two active substances (whose half-lives are different) in a way such that the therapeutically effective period of one drug overlaps at least about 70 % of the therapeutically effective period of the other drug.

In this regard, it also has to be taken into account that there is not a single passage in FANARA wherein the duration of action of any active substance relative to the duration of action of another active substance that is present in the same dosage form is addressed. Whenever combinations of active substances are mentioned in FANARA these combinations are to be contained in immediate release/controlled release dosage forms, i.e., dosage forms which are designed for the sole purpose of providing different release rates and/or release periods of the active substances, i.e., without any concern regarding the time and duration of action of one active substance in relation to the time and duration of action of the other active substance. This fact alone makes it apparent that FANARA is unable to render obvious the subject matter of claim 117, i.e., a claim which addresses, in terms of plasma concentrations within a therapeutic range, the relationship (overlap) between the time and duration of action (period of therapeutic

effectiveness) of one particular (first) type of drug (i.e., a morphine derivative having antitussive activity) and the time and duration of action of another (second) drug which is comprised in the same dosage form and has a half-life that is different from the half-life of the first type of drug.

Applicants further note that the Examiner apparently was unable to cite any document which in combination with FANARA could be considered to render it obvious to one of ordinary skill in the art to use the immediate/controlled release dosage forms set forth in FANARA for providing a plasma concentration within a therapeutic range of one drug over a period which is coextensive with at least about 70 % of the period over which the plasma concentration of any other drug (and specifically, a morphine derivative having antitussive activity) is in the therapeutic range, let alone in a situation where the half-lives of the drugs are different.

Applicants submit that for at least all of the foregoing reasons and the additional reasons set forth in the Appeal Brief filed October 20, 2008 and the Reply Brief filed August 25, 2009 the Examiner has failed to establish a *prima facie* case of obviousness of the subject matter of any of the claims of record in view of FANARA. Accordingly, the rejection of claims 117-119, 134-139, 166, 167, and 175-179 under 35 U.S.C. § 103(a) over FANARA is without merit and should be withdrawn, which action is respectfully requested.

Response to Rejection of Claims under 35 U.S.C. § 103(a) over FANARA in View of JAEGER and FINDLAY

Claims 120-123, 128-133, 140-153, 155-157, 159-165, 168-174, 180-195, and 198-200 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over FANARA in view of JAEGER and claims 124-127, 154, 158, 196 and 197 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over FANARA in view of JAEGER and further in view of

FINDLAY. The rejections appear to concede that FANARA alone does not render obvious the subject matter of the rejected claims but alleges that JAEGER or JAEGER and FINDLAY, respectively cure the deficiencies of FANARA in this regard.

These rejections are respectfully traversed as well. Specifically, like FANARA, neither JAEGER nor FINDLAY renders it obvious to one of ordinary skill in the art to provide a dosage form which comprises two different active substances and provides similar or substantially coextensive periods of therapeutic activity of these two different active substances.

Specifically, JAEGER teaches that 6-amino-2-methyl-2-heptanol (heptaminol), a relatively non-toxic compound lacking antitussive effects of its own, can enhance the effect of codeine so that the codeine dosage and the associated side effects may be reduced sharply while achieving a desired antitussive effect (col. 1, lines 11-17). Example 2 of JAEGER describes a three-layer pill wherein each of the layers contains both heptaminol and codeine phosphate. JAEGER also mentions that the compositions described therein may additionally contain antihistamines, expectorants and decongestants. However, it is not seen that this disclosure of JAEGER in combination with that of FANARA renders it obvious to provide the subject matter of any of the rejected claims, and neither has the Examiner provided any explanation in this regard.

Applicants note that with respect to claims 128-130 the Examiner alleges that "one of ordinary skill in the art would use the teachings of Fanara and Jaeger to make a pharmaceutical composition by using drug combinations ... with drugs having different plasma half-lives in order to optimize the release of drugs over time. Drugs that are part of the immediate release would have a different plasma half-life than drugs that are part of the controlled release in order to maintain drug release for optimal therapeutic effect." Page 7, next-to-last paragraph of the

instant Office Action. Regarding claims 131-133, 145, 146, 159 and 161 the Examiner further alleges that "[t]he claim limitations of periods of plasma concentration within the therapeutic range of the second drug being coextensive with at least about 80%, 90% or 95% of periods of plasma concentration within the therapeutic range of the first drug would have been obvious over the different pharmacokinetic profiles taught by Fanara in view of the antitussive codeine composition taught by Jaeger." Paragraph bridging pages 7 and 8 of the instant Office Action.

In response, it is pointed out that the Examiner has not provided any documentary or other evidence to support these merely conclusory statements. Neither FANARA nor JAEGER even mention differences in half-lives of two drugs, let alone teach or suggest that two drugs whose half-lives differ significantly (e.g., by at least about 2 hours) should be combined in a way such that their periods of therapeutic effectiveness are substantially coextensive.

FINDLAY appears to have been cited by the Examiner merely in order to show that it is known in the art that (certain) antihistamines may be formulated together with decongestants, antitussives and the like. This is clearly not a reason for one of ordinary skill in the art to provide the subject matter of any of the present independent claims, either.

In view of the foregoing, it is submitted that even in combination with JAEGER and FINDLAY, FANARA is unable to render obvious the subject matter of any of the present claims, wherefore withdrawal of the rejections under 35 U.S.C. § 103(a) over the combined disclosures of FANARA, JAEGER and FINDLAY is warranted as well and respectfully requested.

Response to Provisional Rejection of Claims on the Ground of Non-Statutory Obviousness-Type Double Patenting

All claims of record are provisionally rejected on the ground of non-statutory obviousness-type double patenting as allegedly being unpatentable of claims of one or more of co-pending application Nos. 10/736,902, 10/939,351, 11/012,267, 11/115,293 and 11/115,321.

Applicants respectfully request that these rejections be held in abeyance until the Examiner has indicated allowable subject matter. Applicants will then decide if the filing of one or more Terminal Disclaimers is warranted.

CONCLUSION

In view of the foregoing, it is believed that all of the claims in this application are in condition for allowance, which action is respectfully requested. If any issues yet remain which can be resolved by a telephone conference, the Examiner is respectfully invited to contact the undersigned at the telephone number below.

Respectfully submitted,
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November 7, 2011
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